REMARKS

New pages 98 to 100 are submitted herewith containing Sequences 1 to 3, formatted in accordance with the conventions set forth by PatentIn. In addition, the specification has been amended herein to insert the sequence identification numbers. No issue of new matter is raised by these new pages and amendments, as they merely represent the sequences set forth in the application as originally filed and their identification.

CONCLUSION

In light of the Remarks and Amendment made herein, Applicants respectfully submit that the claims are now in condition for allowance and requests a notice to this effect. Should the Examiner have any questions, she is invited to call the undersigned attorney.

Respectfully submitted,

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Version with markings to show changes made:

In the specification:

Paragraph that begins on page 63, line 12, has been amended as follows:

A variety of assays can be used to identify or characterize MC receptor ligands of the invention. For example, the ability of a benzimidazole derivative compound to compete for binding of a known MC receptor ligand can be used to assess the affinity and specificity of a benzimidazole compound for one or more MC receptors. Any MC receptor ligand can be used so long as the ligand can be labeled with a detectable moiety. The detectable moiety can be, for example, a radiolabel, fluorescent label or chromophore, or any detectable functional moiety so long as the MC receptor ligand exhibits specific MC receptor binding. A particularly useful detectable MC receptor ligand for identifying and characterizing other MC receptor ligands is ^{125}I-HP 467, which has the amino acid sequence Ac-Nle-Gln-His-(*p*(I)-D-Phe)-Arg-(D-Trp)-Gly-NH_2 (SEQ ID NO:1) and is described in Dooley et al., "Melanocortin Receptor Ligands and Methods of Using Same," U.S. patent application 09/027,108, filed February 20, 1998, which is incorporated herein by reference. HP 467 is a *para*-iodinated form of HP 228.

Paragraph that begins on page 67, line 18, has been amended as follows:

The competitive ELISA method which can be used here is a modification of the direct ELISA technique described previously in =Appel et al., J. Immunol. 144:976-983 (1990), which is incorporated herein by reference. It differs only in the MAb addition step. Briefly, multi-well microplates are coated with the antigenic peptide (Ac-GASPYPNLSNQQT-NH_2) (SEQ ID NO:2) at a concentration of 100 pmol/50 µl. After blocking, 25 µl of a 1.0 mg/ml solution of each mixture of a synthetic combinatorial library (or individual compound) is added, followed by MAb 125-10F3 (Appel et al., *supra*) (25 µl per well). The MAb is added at a fixed dilution in which the bicyclic guanidine in solution effectively competes for MAb binding with the antigenic peptide adsorbed to the plate. The remaining steps are the same as for direct ELISA. The concentration of compound necessary to inhibit 50% of the MAb binding to the control peptide on the plate (IC_{50}) is determined by serial dilutions of the compound.

Paragraph that begins at page 69, line 27, has been amended as follows:

Binding assays are carried out in polypropylene tubes, each tube containing 0.5 ml of membrane suspension. 8 nM of ^{3}H-[D-Ala^{2},Me-Phe^{4},Gly-ol^{5}]enkephalin (SEQ ID NO:3) (DAMGO) (specific activity = 36 Ci/mmol, 160,000 cpm per tube; which can be obtained from Multiple Peptide Systems, San Diego, CA, through NIDA drug distribution program 271-90-7302) and 80 µg/ml of bicyclic guanidine, individual or as a mixture and Tris-HCl buffer in a total volume of 0.65 ml. Assay tubes are incubated for 60 mins. at 25 C. The reaction is terminated by filtration through GF-B filters on a Tomtec harvester (Orange, CT). The filters are subsequently washed with 6 ml of Tris-HCl buffer, 4 C. Bound radioactivity is counted on a Pharmacia Biotech Betaplate Liquid Scintillation Counter (Piscataway, NJ) and expressed in cpm. To determine inter- and intra-assay variation, standard curves in which ^{3}H-DAMGO is incubated in the presence of a range of concentrations of unlabeled DAMGO (0.13-3900 nM) are generally included in each plate of each assay (a 96-well format). Competitive inhibition assays are performed as above using serial dilutions of the bicyclic guanidines, individually or in mixtures. IC_{50} values (the concentration necessary to inhibit 50% of ^{3}H-DAMGO binding) are then calculated. IC_{50} values of less than 1000 nM are indicative of highly active opioid compounds which bind to the µ receptor, with particularly active compounds having IC_{50} values of 100 nM or less and the most active compounds with values of less than 10 nM.

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FEB 1 2 [illegible]
& TRADEMARK

After "claims.", at page 97, line 6, please insert as new pages 98 to 100 (also attached) the following:

SEQUENCE LISTING

<110> Lang, Hengyuan
Pei, Yazhong

<120> Benzimidazole Derivatives and Combinatorial Libraries Thereof

<130> P-HP 3589

<140> US 09/401,004

<141> 1999-09-21

<150>

<151>

<160> 2

<170> PatentIn version 3.0

<210> 1

<211> 7

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<221> misc_feature

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<221> misc_feature

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<223> Phenylalanine with a methyl at the 4 position of the phenyl ring

<400> 3

Tyr Ala Gly Phe Gly
1 5

Please renumber original pages 98 to 131 as pages 101 to 134, respectively.